Understanding the Pathophysiology of metabolic dysfunction-associated steatotic liver disease and Metabolic Syndrome Following Cholecystectomy*

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The aim of this study is to explore the biological and microbial alterations after cholecystectomy that contribute to the pathophysiology of metabolic syndrome and metabolic dysfunction-associated steatotic liver disease (MASLD).

Ethical review	Approved WMO
Status	Pending
Health condition type	Gallbladder disorders
Study type	Observational invasive

Summary

ID

NL-OMON56983

Source
ToetsingOnline

Brief title
Long-term metabolic consequences cholecystectomy

Condition

- Gallbladder disorders

Synonym
cholecystolithiasis, gallstone disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Laparoscopic Cholecystectomy, MASLD, Metabolic syndrome

Outcome measures

Primary outcome

The primary outcome measure is changes in serum Fibroblast Growth Factor 19 (FGF-19) concentration in response to a standardized fat load.

Secondary outcome

Secondary outcome measures are: 1) changes in hepatic steatosis (MASLD) (assessed by ultrasound imaging of the liver); 2) changes in incidence of metabolic syndrome (waist circumference, BMI, blood pressure, glucose intolerance/insulin resistance (glucose tolerance test)); 3) changes in post-prandial bile-salt excursion; 4) changes in incretin response (GLP-1, GIP); 5) changes in lipid spectrum (TC, triglyceride, LDL, HDL, VLDL); 6) changes in glucose tolerance; 7) changes in faecal microbial composition.

Study description

Background summary

Cholecystectomy is currently recommended as the standard treatment for uncomplicated symptomatic gallstone disease. Although it is generally thought that long-term consequences are uncommon, studies suggest an increased risk of developing metabolic syndrome and metabolic dysfunction- associated steatotic liver disease (MASLD). Changes in the dynamics of enterohepatic circulation of bioactive bile salts, and the reduction in metabolic activity of the gallbladder are biologically plausible and may underly the pathophysiological mechanism following cholecystectomy.

Study objective

The aim of this study is to explore the biological and microbial alterations after cholecystectomy that contribute to the pathophysiology of metabolic syndrome and metabolic dysfunction-associated steatotic liver disease (MASLD).

Study design

Prospective case control study.

The study will comprise two treatment arms both containing 20 patients (total of 40 patients).

1. Patients with symptomatic gallstone disease who undergo elective cholecystectomy.
2. Patients with (a)symptomatic gallstone disease that are treated conservatively.

Intervention

At four pre-specified intervals (baseline, after 3 months, 1 year, and 2 years), all enrolled patients will be administered a standardized fat load (whipped cream), followed by systematic collection of postprandial blood samples. Furthermore, patients will complete lifestyle questionnaires, undergo basic physical examinations (including measurements of weight, height, and waist circumference), a computer assisted ultrasound (CAUS) imaging of the liver will be conducted to determine liver steatosis, and faecal samples will be collected.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit, and group relatedness: In this study, participants will be required to make four visits to the Radboud University Medical Centre during follow-up, consuming approximately half a day each time. To alleviate the time burden for patients, we have opted to assess liver steatosis solely through ultrasound imaging. Traditionally, diagnosing MASLD involves a combination of ultrasound and liver biopsy. However, the computer-assisted ultrasound employed in this study allows for determining liver cell fat content without the necessity of a biopsy. This substantially lessens the burden for the patient. Participation in this study poses no risks or side effects, as we do not intervene with the standard provided treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Patients referred to a surgeon with abdominal complaints and ultrasound proven gallstones or sludge (proven before or after referral) subjected to a laparoscopic cholecystectomy or conservative treatment
• Availability of informed consent.
• Age 30-60 years

Exclusion criteria

• Patients with pre-operative signs of complicated gallstone disease (cholecystitis, choledocholithiasis, cholangitis, pancreatitis),
• Signs of cholestasis requiring intervention (e.g. Endoscopisch Retrograde Cholangio- en Pancreaticografie)
• ASA score III (patient with severe systemic disease (e.g. morbid obesity, renal failure) or IV (patient with severe systemic disease that is a constant threat to life)

• Malignancy (excluding skin malignancies: basal cell carcinoma and non-metastatic squamous cell carcinoma)
• History after bariatric surgery or expected bariatric procedure within 2 years.
• History of inflammatory bowel disease.
• History of alcohol abuse (man >3 and women >2 glasses per day)
• Liver disease (i.e. (autoimmune hepatitis)
• Use steatogenic medication (i.e., methotrexate, tamoxifen, amiodarone, and systemic corticosteroids)
• Use of DPP4-inhibitors
• Diabetes mellitus
• Use of antibiotics in the previous 3 months
• Gastro-intestinal surgery in the previous 3 months
• Stoma (small bowel or colon)
• Patients that are lactose intolerant / allergic to dairy
• Known anaemia < 6 mmol/l
• Expected short life span of less than 12 months
- Body Mass Index (BMI) >30

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2025
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO Date:	03-09-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL87032.091.24